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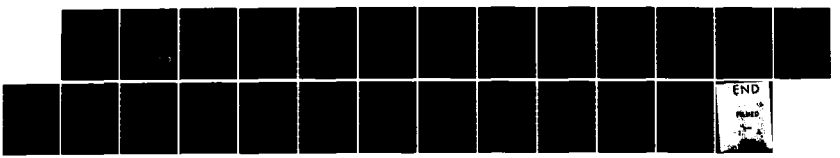

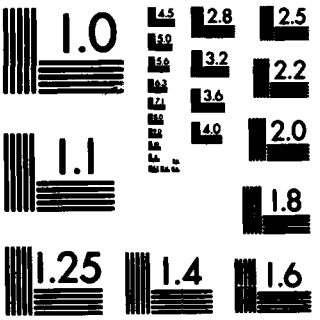

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FUNCTIONAL ASSESSMENT OF LASER IRRADIATION

ANNUAL PROGRESS REPORT

JULY 1975

BY

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The applicability of rhesus behavioral data as an animal model to derive laser safety standards are discussed. While a high degree of morphological and functional similarity exist between the rhesus and human, evidence is presented that the long wavelength sensitivity of rhesus in the fovea is closer to that of the protanomalous observer than the normal human trichromat. These differences possible reflect variations in the distributions of foveal, but not peripheral, receptors and may affect light absorbing characteristics within these species. Recovery data immediately following HeNe exposures are presented.

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INTRODUCTION

The need to establish realistic safety standards for personnel involved in the use of lasers has increased significantly in recent years as a result of the growing employment of these devices in both the laboratory and the field. It is essential that any safety standard establish protect personnel against any accidental exposures which might adversely either the individual's retinal morphology or visual performance. Equally of concern, however, is the usefulness of the intense, coherent irradiation of lasers and the adaptability of the unfiltered human visual system. Overly conservative standards could limit the output power of lasers and hence its usefulness or could require personnel working around lasers to wear protective goggles of such high optical opacity that the visual performance of the user on tasks associated with laser usage could be severely limited. Of course, the ultimate concern must be on the side of safety regardless of the limitations this may necessitate.

Human experimentation in determinations of thresholds for retinal damage, either morphological or functional, is virtually impossible since intentional exposures about the ED50 level can only be preformed on eyes that suffer from severe retinopathies and are slated for early enucleation. Since severe retinopathies are usually associated with substantial loss of vision, often foveal in nature, these patients can describe little about the visual loss associated with laser exposure as opposed to that from preexisting retinopathology (1).

The minimal safety standard which might be employed would protect against exposure levels which would lead to severe and irreversible morphological and functional alterations. Morphological examinations of both human and infrahuman retinas irradiated with intense coherent light will delineate this type of standard. The ultimate set of standards must reflect, however, considerations of the interplay between transitory morphological and functional damage and the safety and performance criteria of specific missions. Indeed, morphological changes alone are of secondary interest, for functional alterations are likely to occur at levels of exposure which do not produce obvious evidence of morphological disruptions. Changes in retinal enzyme concentrations, production of new discs and visual pigments may occur at levels so low that not even microscopic morphological changes are visible.

The limitations associated with the use of human subjects in laser safety studies have resulted in a proliferation of studies in mainly two other species, monkeys and rats. Examination of rat retinas following laser irradiation has been advanced by both the availability of the species for investigation and the minimal amounts of light necessary to produce light-induced retinopathologies. The applicability of these data to humans, however, is questionable. The monkey, on the other hand, because of its morphological and functional similarities to the human (2) would appear to make an excellent animal model for this type of investigation. Monkeys, however, are more difficult to handle and expensive to purchase than the rat and therefore studies on these animals have been somewhat slow to develop.

Light induced pathology in the rhesus monkey retina has been extensively studied for suprathreshold exposure conditions. Both coherent (laser) and incoherent light sources have been used to produce rather massive amounts of damage at various levels within the rhesus eye (3 - 6). While these studies have provided evidence for the site and possible mechanisms of light induced damage they have provided little evidence as to the adverse consequences of this damage on visual performance and even more importantly, on the transitional point between reversible and irreversible damage levels.

Functional studies concerned with the adverse effects of intense irradiation on the visual system have likewise been restricted to the evaluation of severe retinal disruptions of the fovea in the rhesus (7 - 10). The effects of these irradiation levels on the fovea were usually permanent, producing impairment in visual acuity ranging from 40% to 80% of pre-exposure acuity levels. Virtually no exploration of exposure levels at or below the transition from temporary to permanent visual deficits has been conducted prior to our investigation since no technique had been available to expose an awake, task-oriented animal. Immediate acuity changes following exposure are critical in the exploration of both thresholds for functional disruptions and for determinations of the immediate effects of irradiation on visual performance, both above and below those levels associated with permanent functional and/or morphological damage. The inability to measure these transient changes in visual acuity at threshold and subthreshold levels, as well as a means to follow the initial phases of the deficits elicited by suprathreshold power densities, was a serious limitation in all previous studies. During the course of the last several years we have developed a method for producing foveal exposures in an awake, task-oriented animal (11, 12). Associated with this procedure has been the development of a rapid method to measure rhesus visual acuity immediately before and after laser exposure. This method is a modification of that proposed by Graham, Farrer, Crook, and Garcia (10) and has been used in the current investigation to continue the examination of the immediate effects of laser irradiation on rhesus visual acuity.

The applicability of this data on rhesus to humans obviously will depend upon the degree of functional similarity between the species. As noted above, there is a high degree of morphological similarity between rhesus and humans although the rhesus eye is somewhat smaller and more highly pigmented making it perhaps a more efficient collector of light eneergy. Likewise, the ability of rhesus to resolve spatial detail and their sensitivity to color also have been shown to resemble that of the human. Although they are similar differences in the ability of the rhesus to resolve spatial detail under different achromatic luminance conditions have been reported (13). These differences in effective luminances were attributed to optical rather than physiological factors. Comparative chromatic studies have also generally shown the rhesus to be similar to the human although again slight differences have been reported. These differences have likewise been accounted for solely by variations in optical transmission and accommodation between the two species, and have not been attributed to differences in either receptor or neural function. Sidley et al. (14) and Schrier et al. (15), for example, both report that the short wavelength sensitivity of the rhesus is superior to that of the human under photopic conditions. Slight differences in sensitivity in

this spectral region could be attributed to the greater short wavelength transmission of the rhesus lens and macular pigment (16, 17). Under comparable scotopic conditions, however, Blough and Schrier (18) reported a better overall agreement between the rhesus and human although under these luminance conditions the rhesus was now slightly superior in the long wavelength region of the spectrum. On the other hand, Grether (19) reported evidence suggesting the rhesus requires more "red" (610 nm) light in a complimentary color mixture to match "white" than do normal human trichromats. In a more recent study using acuity discrimination, rather than absolute threshold, Behar and Bock (20) have also reported that the long wavelength sensitivity of the rhesus is inferior to that of the normal human observer when fine grating targets are employed. These long wavelength differences were attributed to species differences in accommodative power.

In all previous studies, the test targets were typically either not defined on the retina (animal free moving) or were spread across a wide portion of the retinal mosaic if head and eye movements were controlled. In no studies were the spatial resolution characteristics of the paradigm such that only foveal cone function could be isolated and tested directly. Recent comparative anatomical evidence suggests that the rhesus retina may contain fewer foveal cones but more parafoveal cones than the human (21) although it must be mentioned that the overall topography of rods and cones within the human and rhesus retinas closely resemble one another. Some of the inconsistencies present in the literature regarding the similarities and/or differences in rhesus and human spectral sensitivity perhaps may be related to the proposed differences in cone densities across the retina in addition to the purely optical factors already discussed. During a portion of the current effort, we have attempted to measure the spectral sensitivity of rhesus using a Landolt ring acuity task which relates more specifically to small and more defined regions of the central fovea. By restricting chromatic visual functioning to the central most regions of the retina, new evidence is presented suggesting that the rhesus photopic color vision is more protanomalous than previously reported. Such a condition will affect the light absorbing properties of the photoreceptors within the fovea and, given the thermal model for retinal damage thresholds, the tolerance of the retina particularly to long wavelength irradiation.

During the course of this project we have also continued exposing animals to a HeNe source and derived recovery functions for both threshold and subthreshold energy densities on the retina. Continued HeNe exposures were important to increase the size of the sample on this particular exposure paradigm. We have begun the task of converting to a Krypton laser which will allow us to examine the effects of exposed retinal area on the magnitude and duration of the recovery. In addition, our new laboratory facilities have been completed and we moved from our temporary facility to the new complex during this support period. These new facilities will allow us to run more animals per day and reduce the interference of noise and light during training and testing.

METHODS

SUBJECTS. Four rhesus monkeys (Macaca mulatta) served as subjects in this experiment. All animals were housed and tested in modified primate chairs. Each animal was refracted by means of retinoscopy before testing, and no significant refractive errors were found. Four normal human trichromats and two protanomalous humans were also used for comparisons of spectral sensitivity. All human observers had clinically normal vision and were screened for color vision deficits using Ishihara Tests for Colour Blindness and the American Optical Corp. Pseudo-Isochromatic plates. These tests were used to nominally differentiate a human group with long wavelength deficiencies.

APPARATUS. Animals were tested for visual acuity in a light-tight, primate cubicle isolated in a separate room from the programming equipment. During the initial stages of this effort the entire laboratory was moved from a classroom which served as a temporary laboratory during the transitional contract (DAAA25-74-Q0587) to a new facility constructed exclusively for this project. A portion of the effort expended during this time period involved moving the equipment, realigning and calibration of the optical/laser system. Also during this period, new solid state programming equipment was purchased and installed to replace the old electromechanical equipment previously used at the Eye Research Foundation (Contract No. DAAA25-71-C-0497). During the course of the early efforts in this project this equipment became quite unreliable due to mechanical brakedowms and many hours were spent in an attempt to diagnosis specific problem circuits. Temperature and humidity greatly affected the timing sequences of the relays and often caused temporary problems which delayed data collection. The acquisition of the new equipment and its installation will greatly reduced the time spent diagnosing and reprogramming the equipment during the course of future efforts.

The test chambers used during this effort were essentially the same as previously used although some minor rewiring was necessary as a result of the new programming equipment. A high-resolution, rear-projection screen (Polacoat Co.) was mounted on the far wall of the cubicle and aligned with an artificial pupil placed in the subject's line of regard. The screen subtended 3 x 3 deg at a distance of 1 m from the subject's pupil. Maximum background luminance of the test screen was 2.5 x100 cd/m2.

The test patterns were conventional black Landolt rings presented against a light background. The advantage of the Landolt ring over grating targets is that the break in the ring relates more specifically to small and more defined retinal regions (23). The rings were printed on Kodalith film (Eastman Kodak Co.) and when projected yielded a luminance contrast of approximately 97% between the rings and the light background. Background luminance and color were modified with neutral density and interference filters placed in the optical pathway. The thickness of the Landolt rings and the width of the gap that formed the critical detail were always 1/5 of the diameter of the ring, and the size of the gap was varied photographically from a projected 0.25 to 30 minutes of visual angle in equal 20% steps. The Landolt rings were presented in sets of four gapless rings that were of equal ring diameter. The position of the Landolt ring among the gapless rings was randomly set.

The subject's head was held in place 1 m in front of the screen by four Plexiglas head restraints mounted on the animal's primate chair. These restraints prevented head movements in any direction. An opaque facemask and 7.0 mm monocular iris diaphragm was aligned with the subject's pupil and viewing screen so that eye position could be well controlled during testing. All discriminations were made under monocular viewing condition and with natural pupils. Except for the screen, the entire test chamber and surrounding room were entirely dark.

DISCRIMINATION TASK. The subject's task was to respond to the Landolt ring pseudorandomly placed within a series of equal diameter gapless rings. The apparatus and paradigm, with exception of the presentation of shock to the rhesus for incorrect detections, was the same for all three classes of subjects. Each ring was projected for 2 seconds and there was a 1 second dark interval between successive rings. No special cue was given when a set began; the stimuli appeared to the subject as a single long series.

The rhesus subjects were trained, using negative reinforcement, to press a lever whenever a Landolt ring was presented and not to respond when gapless rings of the same dimensions were presented. If the subject failed to respond to the Landolt ring during the 2 second presentation, he received a brief electrical shock through an electrode in the seat of his Plexiglas primate chair. Shock was produced from the secondary of a high-tension coil by discharging a capacitor into the primary; it was annoying but not highly painful or dangerous because of its extremely short duration. To discourage the subject from responding indiscriminately to all rings, every third lever press during gapless ring trials was also followed by shock. Training to threshold acuity levels took from 4 weeks to 3 months depending upon the cooperation of the subject. Discrimination training began on light vs dark Landolt rings and the animal was gradually shaped to make the required discrimination based on form rather than intensity.

Threshold acuity measurements were obtained by a tracking method which allowed the subject to adjust in discrete steps the size of the test object about his own threshold. The size of the gap in the ring increased following incorrect Landolt ring responses and decreased following correct Landolt ring responses. Lever responses on gapless ring trials did not affect the size of the gap to be presented on the next series of trials. Means and standard deviations of the threshold visual acuity were obtained by the use of Dixon and Massey's statistics for the tracking method (23). When threshold acuity was measured in rhesus following laser exposure, the average number of completed rings relative to Landolt rings was reduced to two. Reduction in the number of completed rings relative to "target" rings has allowed us to more quickly track transient changes in visual acuity as a function of time after exposure. Baseline mean levels or variability have not been affected by changes in the ratio of Landolt rings to completed ring trials. Also unaffected were the number of lever responses during completed trials which was always very low in our subjects (see Figure 4).

LASER SYSTEM. In previous projects, a standard 50 mW HeNe laser served as the exposing source. During the course of the current project a second 2 W Argon laser with a Krypton plasma tube has been installed. A second optical system for this new laser system has been constructed along side

of the previously used system. This new laser and associated optical system will allow us to adjust the diameter of the laser spot on the retina. With the HeNe laser the largest diameter exposure on the retina of sufficient power density to produce either a functional or morphological disruption was 200 microns. Larger spots capable of permanent functional alterations can now be produced by the new Krypton laser because of its higher output power. Variations in spot size can be produced by different expansions of the coherent beam through an afocal telescope. In addition, the Krypton laser will permit testing of different monochromatic recovery functions using different spectral lines provided on the system. Exposures with different spectral lines, however, will have to be made with the smaller diameter beams since the energy densities in these other spectral regions will not be of sufficient power densities to produce a lesion when expanded.

A diagram of the optical system is shown in Figure 1. The entire laser system, with exception of a final focusing lens and beam splitter has been mounted outside the experimental chamber. The "raw" beam past first through a manual safety shutter and electronic shutter which produced a calibrated exposure of 100 msec. The beam was then attenuated by neutral density filters. The attenuated beam was diverted by a 4.5 cm diameter

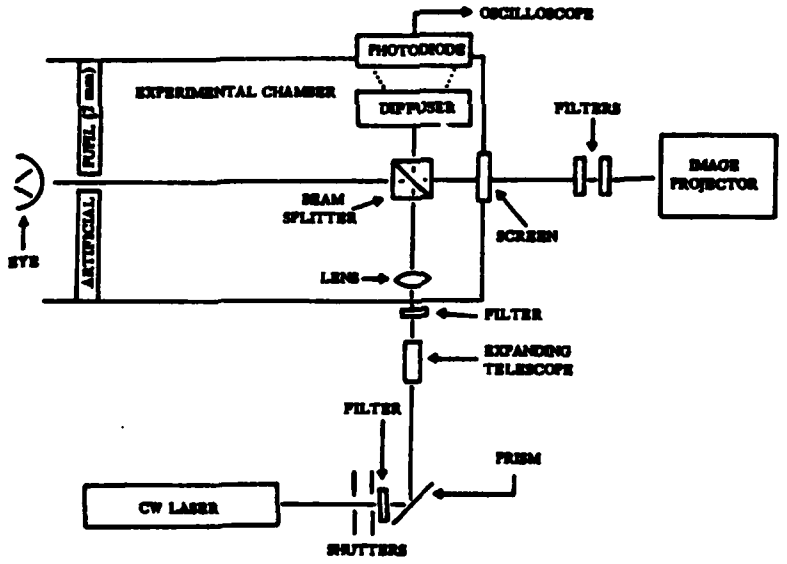

Figure 1. Optical system used to present image targets and to expose the animal to large diameter spots using a Krypton laser.

front surface mirror and entered a beam expanding telescope which produced a collimated beam of adjustable size between a minimal spot of 50 microns and one greater than 500 microns. The expanded beam then past into the experimental chamber and through a 1.25 diopter lens placed 85 cm in front of the subject's pupil. A 5 x 10 cm coated pellicle beam splitter was

placed 5 cm in front of the lens and at the intersection of the diverging laser beam and beam from the carousel projector. Mounted on the opposite side of the beam splitter was a diffuser and ultrafast photodiode (HPA 4203). The output of this detector was displayed on a memory oscilloscope and was regularly calibrated against an EFF Model 580 Radiometer placed at the corneal plane. The power and pulse width of each irradiation was measured and recorded.

The laser exposure was presented to the animal coaxial with a line between the artificial pupil and the gap in a specified Landolt ring subtending less than 1 minute of arc (threshold target). For determination of the line of sight, a 2 mm aperture was placed on the screen over the gap and a 4 mm aperture was placed at the plane of the cornea. A mirror, approximately 2 m behind the 4 mm aperture was adjusted until it was normal to the line of sight. The beam splitter was then aligned such that the collimated beam from the laser past through the 4 mm aperture and was reflected off the mirror back onto itself. Coaxial alignments with the line-of-sight was verified by noting that the reflected beam also passed through the 2 mm aperture and onto the discriminanda on the screen.

LASER EXPOSURE. Prior to any laser exposures, stable baseline acuity levels were established for each subject. During the course of this effort four animals were trained and stable thresholds determined. A criterion of, at minimum 14 consecutive sessions of threshold measurements were used to establish a baseline mean and standard deviation for each stimulus condition. Prior to each exposure, a 15 minute baseline session was made and the mean for this pre-exposure session determined. The number of completed ring trials was then reduced and comparisons made to assure a stable baseline. Failure of the subject to obtain a mean acuity level within one standard deviation of his predetermined baseline level on either schedule aborted the session. Session variability which exceeded baseline variability also aborted the session.

All exposures were made during threshold measurements after the above criteria were met. The laser exposure was triggered by the animal's correct detection of his threshold Landolt ring which corresponded to a gap size of between 1.0 and 0.5 minutes of visual angle. A electronic shutter was automatically triggered by a microswitch on the response key. Casual observations of numerous animals working under similar conditions have revealled that subjects maintain fixation during their response period. The results of the data collected thus far during the current effort support these conclusions. Voluntary eye movements or blink during laser exposures were eliminated by the use of a 100 msec exposure duration. Exposures were made over power levels from 1.0 mW to 15 mW with the lowest power level presented first. No more than one exposure was made per session and exposures were never made either following incorrect detections of Landolt rings or during the last 1 second of the trial.

Immediately after exposure, recovery was measured until the subject returned to baseline acuity levels. The session was terminated after a 15 minute stable baseline was achieved. The entire test session lasted approximately 2 hours. Under conditions where total recovery was not complete within 2 hours, the session was terminated and no exposure was made the following or subsequent sessions until a stable baseline was again achieved.

RESULTS

Sample baseline acuity data for one animal is shown in Figure 2 for several different intensity levels of background luminance. All measurements were made after an initial period of dark adaptation and under maximum (97%) contrast conditions. Acuity was defined in the usual manner as the reciprocal of the visual angle subtended by the gap at threshold and list in Snellen terminology on the right hand margin of the figure. For each plot, vertical digressions were reversals in the strip chart recorder controlled by a potentiometer mounted on top of the carousel image projector and hence represent changes in the size of target

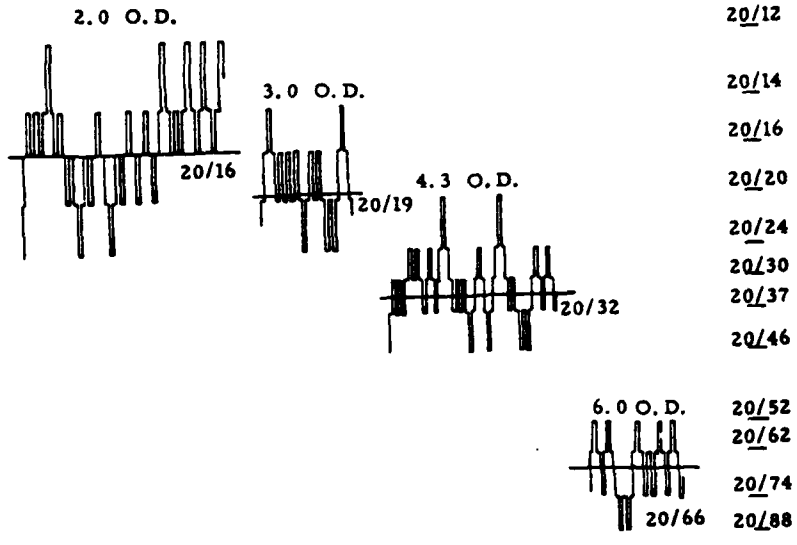

Figure 2. Raw strip chart data on the effects of background luminance on acuity for one rhesus monkey. Horizontal pen excursions represent Landolt ring presentations; vertical pen excursions represent gapless ring presentations.

on the screen. As previously discussed, the size of the target was contingent upon the subject's correct detection of a previous Landolt ring; correct detections were followed by a smaller series of rings (upward digressions) and incorrect detections were followed by a larger series of Landolt rings and gapless rings (downward digressions in the figure). Horizontal digressions in this figure represent the actual presentation of the Landolt ring within the series of gapless rings. Four different background luminance levels are presented in this figure. For a background level of 2.0 log units (2.0 O.D.) below our maximum photopic

condition, mean acuity for this animal was 1.25 (min. of arc)-1 or a Snellen acuity of 20/16. Reduction of the background luminance by an additional 4.0 log units (6.0 O.D.) resulted in an acuity level of 0.303

(min. of arc)-1 or a Snellen acuity of 20/66. As evident in this figure, variability within a session was quite small. When acuity was plotted against background luminance across a wide range of values for either achromatic or chromatic targets, a very strong correlation (consistently in the order of .90 or above) between the two variables existed.

Sample intensity-acuity functions for one subject are presented in Figure 3 over a five log unit range for various chromatic backgrounds throughout the visible spectrum. The slopes of the regression lines shown in this figure are somewhat shallower for the shorter wavelengths (420 -500 nm)

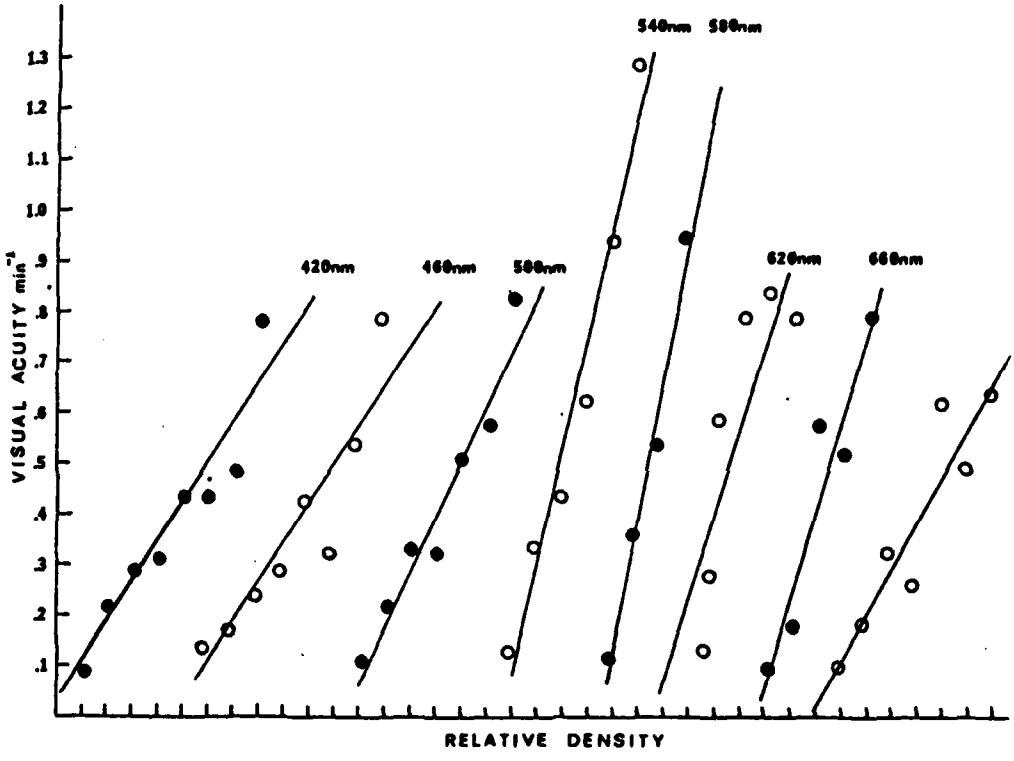

Figure 3. Monochromatic intensity-acuity functions for one rhesus subject. The data points represent the mean acuity of several different sessions and the line drawn through the data represents a least square line for this data.

than for the intermediate (520-620 nm). In the longer wavelength region (620-700 nm), the slopes of the functions were also shallower than those for the shorter wavelengths. The steepest slopes for the regression lines were found for the intermediate region between 540 and 580 nm. Slight discontinuities from the linear regression lines in the short wavelength region of the spectrum (420-500 nm) at acuity levels of 0.3 (min of arc)-1 are observed in this figure and also were found in the same spectral regions for other animals. For all other regions of the visible spectrum the data conformed nicely to a linear equation across a large dynamic range often in excess of 10 log units of background luminances.

Using a signal detection approach to the analysis of the subject's behavior during threshold discriminations, our subjects were always very conservative in their discriminations. This was particularly true of our animal subjects due to the payoff matrix (negative reinforcement of misses and false alarms) used in the study. The percent correct detections of both Landolt rings and gapless rings for one subject is shown in Figure 4. In this figure the percent correct detection of each type of target is plotted against the log of the reciprocal of the visual angle (visual acuity). This data suggests that our animals do not "guess" by pressing the lever whenever the targets become very small. On the contrary, the percent correct detection of gapless rings (a null response condition) remains consistently above 90% regardless of the acuity level of the target. What did vary with different size targets was the correct detection (initiating a lever response) of the Landolt ring.

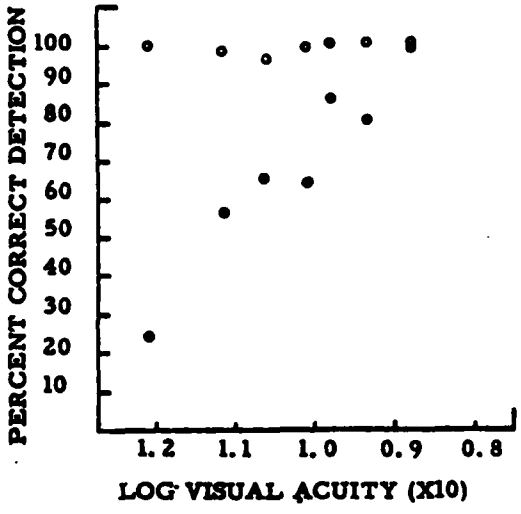

Figure 4. Percent correct detections of Landolt rings and gapless rings are plotted for different size targets. The open circles represent the data for gapless rings while the filled circles represent the data for Landolt rings. The subject in this figure was a rhesus monkey and the data present averages over several sessions.

Sample raw acuity data from our tracking technique are shown in Figure 5 for the normal trichromatic human, the rhesus, and the protanomalous human. These graphs are similar to those presented in Figure 2 but represent the raw data for three different types of subjects for one background wavelength and luminance. At this wavelength and background luminance level the absolute acuity of the normal human was greater than that of either the rhesus or the human protanomalous observer. Similar relationships in absolute sensitivity did not exist when different wavelengths and luminances were employed as the background for the Landolt rings and gapless rings. Background wavelengths were shifted in 20 nm steps throughout the visible spectrum over a range of at least 5 log units

of luminances for each subject. Spectral sensitivity curves were derived in the customary manner from these data. A minimum of 15 minutes of threshold measurements at each luminance level were made for each wavelength and were repeated over a minimum of 4 different test sessions. A counter-balanced design was used.

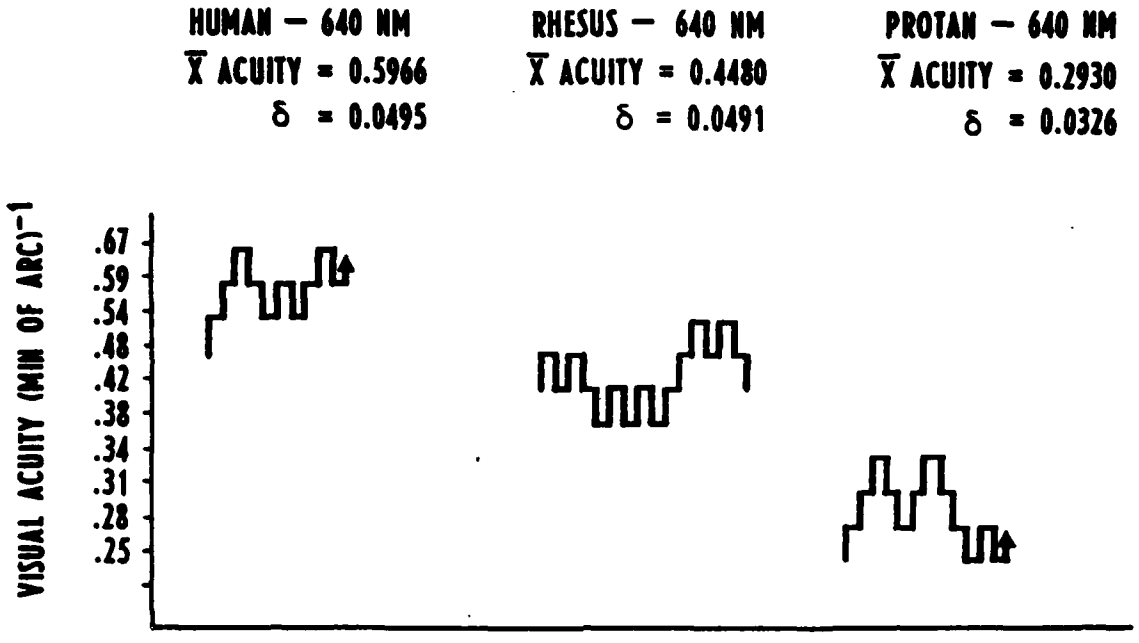

Figure 5. Sample raw data of the acuity levels of normal human observers, protanomalous human observers and rhesus monkeys to a similar background wavelength and luminance condition.

Comparisons of maximum spectral sensitivities for the rhesus, normal human and protanomalous human showed rather broad peak sensitivities between 520 and 560 nm when normalized at 540 nm. No significant shift in peak spectral sensitivity was noted across the relatively wide range of criterion acuities selected for any group of subjects although changes for all were apparent in the breadth of the curves. In the long wavelength region of the spectrum beyond 520 nm, the sensitivity of the human trichromat and the rhesus were nearly identical for the coarsest criterion presented (0.11 min-1) and both were nearly one log unit more sensitive than the human protanomalous in this spectral region (see Figure 6). The overall shape of the curves for the normal human and rhesus were similar to those reported by Sidley et al. (14) and Schrier and Blough (15). This relationship, however, altered as criterion acuity became finer. With a finer criterion of 0.52 min-1 (Figure 6,B) the rhesus sensitivity to the long wavelength region was about 1 log unit less sensitive than that of the normal trichromat, the long wavelength sensitivity of the rhesus now being nearly identical to that of the human protanomalous. In both of these groups of subjects the long wavelength sensitivity differences were statistically different from the normal human observer.

At our finest selected criterion acuity (1.11 min-1)(Figure 6 C), the rhesus was as much as 2.0 log units less sensitive than the normal trichromat and even less sensitive than the human protanomalous in this region. For short wavelengths, however, the rhesus and the human protanomalous sensitivities were similar across most acuity criteria and both were slightly more sensitive than that of the normal trichromat.

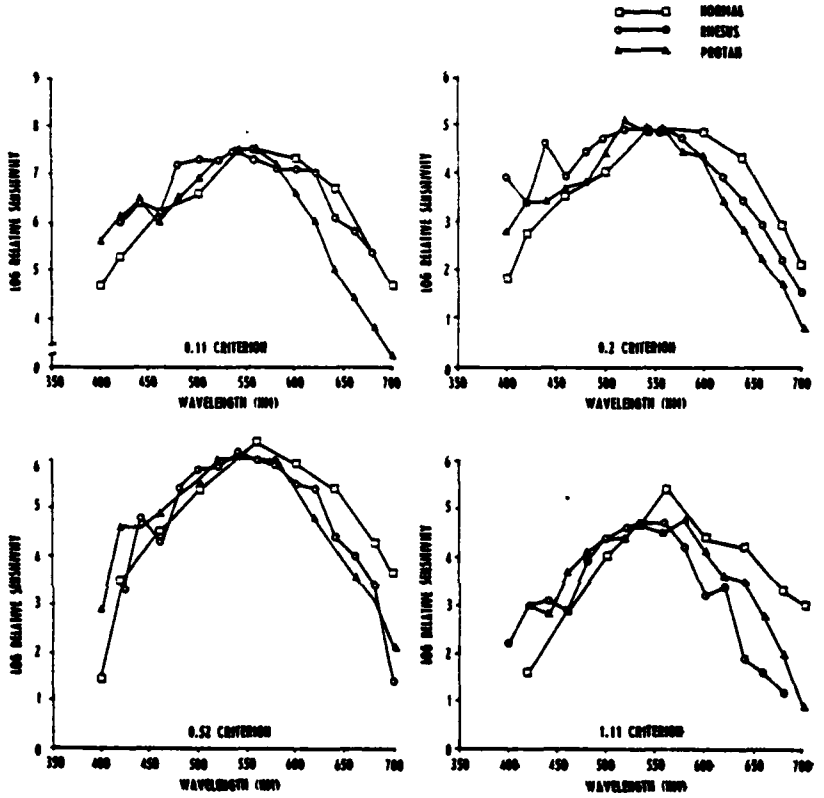

Figure 6. Comparisons of the mean spectral sensitivities for three criterion acuities. In each graph, the mean spectral sensitivity for a given criterion acuity is shown for human trichromats, rhesus, and human protanomalous subjects. For each selected criterion acuity, all spectral sensitivity curves were equated at the 540 nm point which was the usual maximum spectral observed for all groups of subjects. Comparisons made on an absolute basis yielded similar results. Each data point represents the interpolated sensitivity corrected for quantal output as derived from the mean regression equation of the combined individual intensity acuity function for each wavelength and for each subject.

A statistical comparison of the curves for all three groups of subjects and wavelengths is presented in Figure 7. Statistical comparisons based on pooled t-tests were derived for all three criterion levels. As the

tables show statistically significant differences were observed between the rhesus monkey and normal humans subjects at high but not low criterion levels in the long wavelength region of the visible spectrum. In this same spectral region at the highest criterion level there were no statistically significance differences between the rhesus and the protanomalous human subjects. At lower criterion levels there was statistically significant differences between the normal trichromats and protanomalous human observers but no significant differences across an wide spectral region between the rhesus and either group of humans. At the lowest criterion level the rhesus was also significantly more sensitive to the short wavelength region of the visible spectrum than was the normal human trichromat.

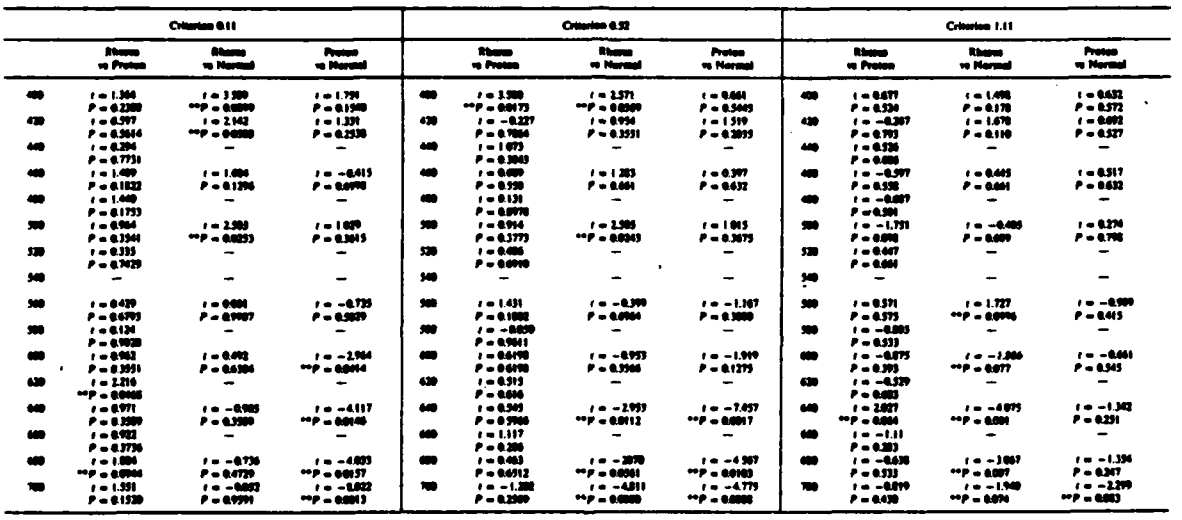

Figure 7. Statistical comparisons (pooled t-tests) of the mean sensitivity differences for all groups of subjects at each presented stimulus wavelength and across the three criterion levels shown in Figure 6. The asterisks indicate P values greater than the 0.10 level.

In one animal exposed to 100 msec flashes from HeNe laser using a relatively small spot of 150 microns on the retina, recovery time was dependent upon the energy of the flash. In Figure 8 is shown the individual recovery functions for six different power levels ranging from 1.7 mW to 11.0 mW. Total recovery time varied from less than 4 minutes when low power densities (1.7 mW) were used to greater than 15 minutes when higher power densities were used (greater than 7.0 mW). For power levels above 11.0 mW, recovery was not complete within the two hour test session and as seen with other animals, recovery following repeated exposures at this power level became progressively longer until recovery was no longer complete.

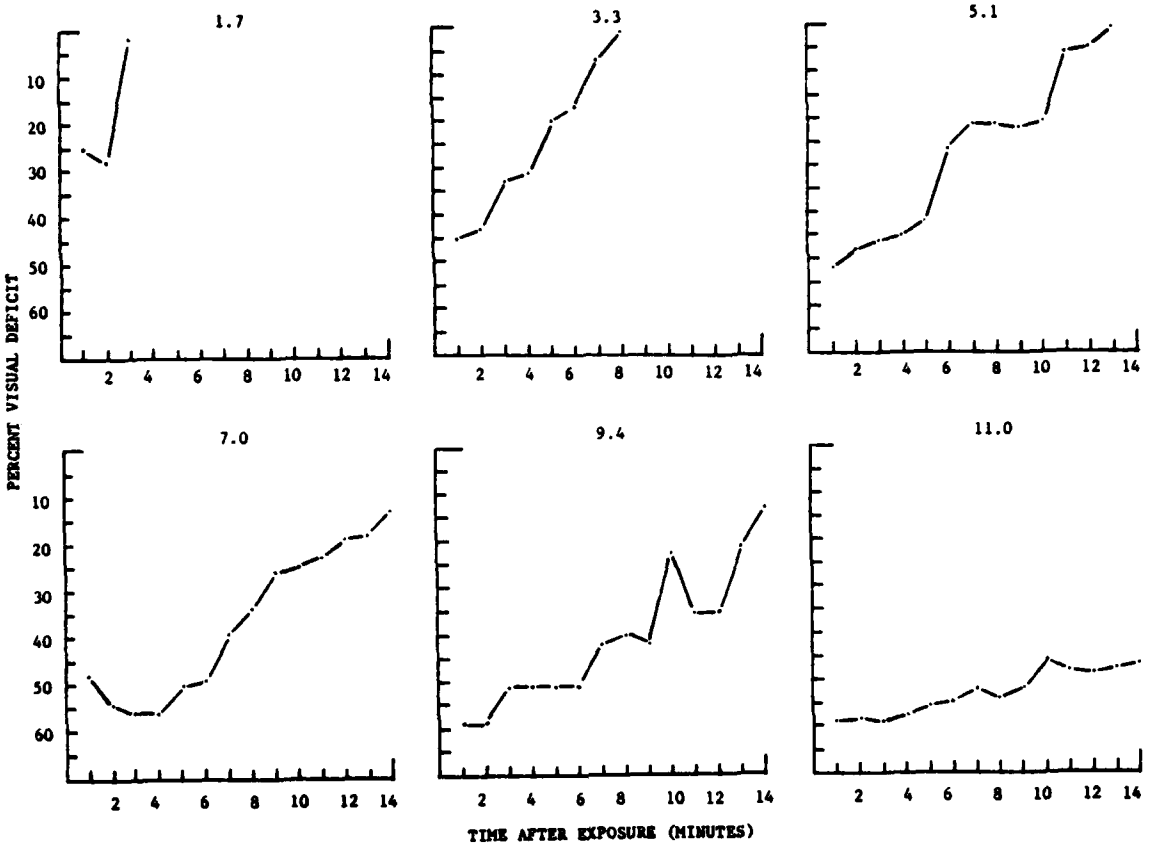

Figure 8. Percent deficit in visual acuity from pre-exposure baseline acuity following exposure to HeNe flashes of various power densities.

As can be seen in the above figure, exposure to laser flashes of various power densities produce an immediate, but often temporary, deficit in visual acuity. The size of the initial deficit in acuity was independent of power level over a range of 1 log unit below levels that produced permanent functional deficits. For relatively small diameter exposures on the retina (150 microns), the initial acuity deficits ranged from 0.59 to 0.44 (min of arc)-1 which corresponded to acuity deficits of 40 to 60% of pre-exposure baseline levels. With larger diameter exposures to be used in the next portion of this study we will expect to see larger initial deficits and perhaps longer recovery times. The recovery process consisted to two distinct stages especially when higher power densities were used. The initial stage was a rather consistent depressed sensitivity immediately following exposure. During this period no significant changes in acuity occurred over time. The second stage of the recovery process was a gradual recovery in acuity over time back to the animal's pre-exposure baseline acuity level. The duration of the maximum deficit (stage 1) and the total time required for recovery (stage 2), however, were directly related to exposure power. In Figure 9 recovery times for both the initial portion of recovery from the maximum deficit and the total time for full recovery is shown.

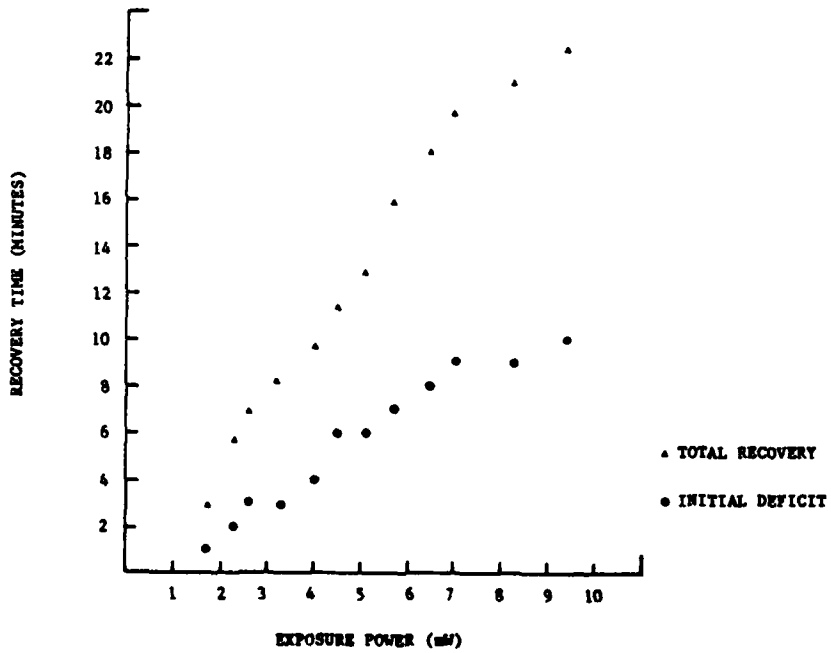

Figure 9. Recovery time following 100 msec exposures to 150 microns spots on the retina of various power densities. The filled circles represent the time required before the animal began to recover from the initial maximum deficit elicited by the laser flash (stage 1). The open triangles represent the total time required for the animal to return to his pre-exposure, baseline acuity level. Each data point represents the mean of at least three different exposures over an equal number of test sessions.

DISCUSSION

In relation to the appropriateness of the rhesus as a animal model for our functional study of retinal damage, the comparisons of spectral sensitivity of humans and rhesus suggest several points of concern. When using relatively coarse acuity criteria in determining spectral sensitivity, the relationship between the rhesus and normal trichromat sensitivity is similar. This similarity between the two species corresponds nicely with the data of Behar and Bock (20) for their maximum acuity criteria. The criteria involved, however, are relatively coarse and could correspond to the sensitivity of parafoveal vision and not necessarily central foveal vision. In our study when even finer criteria were used which required foveal vision, the rhesus was as much as 2.0 log units less sensitive than the normal trichromat to the long wavelength region of the visible spectrum. The rhesus was, in fact, even less sensitive under these conditions than protanomalous humans.

The reason for the rhesus long wavelength insensitivity is still unclear. Several optical factors could cause differences in relative sensitivities between the two species although it would be difficult to conceive optical factors alone causing the large decreases in rhesus long wavelength sensitivity. The slightly greater spherical aberrations of the rhesus eye as compared to that of the human may explain the overall ability of normal humans to resolve finer detail than rhesus but does not explain the increasing loss in long wavelength sensitivity as the task required more foveal fixation. Likewise, differences in the macular pigment and the transmission of the lens which exist between the two species might explain differences in short wavelength sensitivities but can not be expanded to explain the observed differences in the long wavelength region of the spectrum.

The fact that this long wavelength insensitivity, relative to the normal human observer, is apparent only when very fine acuity targets are presented and not for all acuity criteria like in protanomalous humans suggests differences in either the distribution of or interconnections between long wavelength receptors within the foveal or parafoveal areas since acuity ultimately must depend upon these factors. Previous investigators (20) attributed similar findings to a possible accommodation difference between the rhesus and human. Our experimental paradigm minimized this factor by having an almost constantly illuminated screen, a fixed head position, a relatively long viewing interval, and a viewing distance of 1 m. In addition, the magnitude of our observed long wavelength insensitivity was much greater than that previously reported when finer acuity targets were used which required central foveal fixation and function. Hence, our results become more difficult to explain by a purely optical mechanism as suggested by other investigators (14, 15, 20) and imply physiological differences between the two species especially when foveal function is considered.

The observed increased short wavelength sensitivity in the rhesus reported in this study is reminiscent of the results of previous investigators and might be partially explained in rhesus on the basis of species differences in spectral opacity of the lens and macular pigmentation. In the human protanomalous subjects, the slight increase in sensitivity to short

wavelengths noted here and elsewhere may be caused by a reduction in the amount of neural inhibition on blue receptors from a now reduced population of red receptors (25) although such an explanation may be better for an acquired rather than a congenital state. These short wavelength differences between normal and protanomalous human observers were not statistically significant although differences between the normal human observers and rhesus in this spectral region for low acuity criteria were statistically significant.

All of the comparisons made in this study were based on mean spectral sensitivity curves equated at 540 nm. Obviously the selection of another spectral point to equate our curves would have drastically altered our comparisons although the magnitude of the effect would have still lead to the conclusion of differences in foveal organization between the human and rhesus. The selection of the 540 nm point, however, was not arbitrary on our part. First, it corresponded to the maximum spectral sensitivity observed for all of our subjects. Second both our absolute data as well as that of Behar and Bock (20) demonstrate that the long wavelength sensitivity of the rhesus for high resolution criteria is significantly less than the human trichromat. To normalize our spectral sensitivity curves in the long wavelength region of the spectrum would have ignored this important observation. And thirdly, if our functions had been normalized beyond 620 nm, not only would the rhesus have become significantly more sensitive than the normal human trichromat below 520 nm, but so also would have our human protanomalous observers. A moderate increase in short wavelength sensitivity in rhesus and human with altered spectral sensitivities might be a reasonable expectation as discussed earlier, but how could one account for such large differences in human foveal short wavelength sensitivities without negating the absolute long wavelength differences between our different classes of human observers?

Regardless of whether the differences between rhesus and humans is the result of optical or physiological factors or some combination, our data suggest that caution should be exercised when using the rhesus as a prototype for human foveal color vision. This is partically important in studies where thermal factors are critical in determining the effects of light absorption on visual performance and sensitivity. Differential photopigments distributions, receptor densities, or macular pigmentation could alter the adverse effects of intense irradiation on visual functioning. Our results indicate that the observed differences in primate sensitivity are in some way a function of different foveal and not peripheral factors that exist between these primate species. Since all of our exposures have been foveal and our sensitivity measures photopic, the above factors become important considerations in relating the rhesus laser exposure data to humans.

Exposure of rhesus to brief laser flashes significantly below the ED50 level produced an immediate and often temporary deficit in acuity. Repeated exposures at relatively low power densities eventually produced permanent changes in visual sensitivity to high resolution targets. The magnitude of the maximum acuity deficit in this experiment is consistent with those studies where permanent foveal disruptions were produced (7, 9) and suggest foveal involvement. These deficits are consistent with the manner in which exposures were initiated, that is, during measurements of maximum acuity under photopic conditions where involvement of the central

most area of the retina was required. Our results imply that in our paradigm our animals maintained fixation on the discriminanda immediately following their overt behavioral response in the vast majority of trials. These data support the appropriateness of our behavioral paradigm in carrying out the stated missions of the protocol. In a few cases, laser exposures elicited little or no acuity deficits. In these cases it might be suggested that eye movements or lid closures resulted in either irradiation of extrafoveal areas or reduced foveal involvement. Since these occurrences were minimal (less than 25% of the time) we believe we have developed an effective behavioral paradigm to centrally expose task-oriented animals and immediately measure any changes in visual sensitivity produced by such exposures. In subsequent efforts, this method will be used to extend our current results to other animals, exposure paradigms, and performance tasks.

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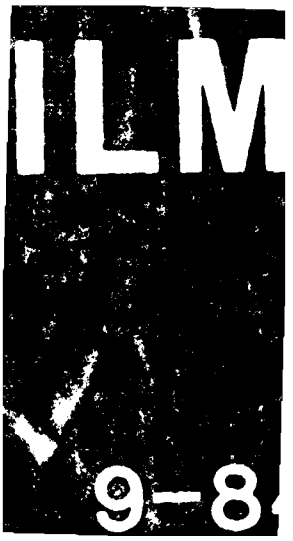
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